

CORRELATION BETWEEN PAI-1, LEPTIN AND FERRITIN WITH HOMA IN HIV/AIDS PATIENTS

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INTRODUCTION:

The introduction of combined antiretroviral therapy (cART) in HIV/AIDS patients has dramatically decreased progression to AIDS and importantly lower death rates. However, cART has been associated with a number of adverse events such as lipodystrophy, insulin resistance (IR), diabetes mellitus (DM) and hyperlipidemia, with an increasing risk of cardiovascular disease (CVD) and metabolic syndrome (MS).

Data about correlation of interleukins (IL-1 α , IL-1 β , IFN γ , IL-2, IL-4, IL-6, IL-8, IL-10), adipocytokines (leptin, adiponectin, monocyte chemoattractant protein-1 (MCP-1), resistin, plasminogen activator inhibitor-1 (PAI-1), tumor necrosis factor alpha (TNF α), ferritin, C reactive protein (CRP) and vascular endothelial growth factor (VEGF) with homeostasis model assessment (HOMA) in HIV/AIDS patients are still limited. with combined antiretroviral therapy (cART).

AIM:

The aim of this study was to evaluate the possible correlations of following serum interleukins: IL-1 α , IL-1 β , IFN γ , IL-2, IL-4, IL-6, IL-8, IL-10 levels, adipocytokines (leptin, adiponectin, MCP-1, resistin, PAI-1, TNF α), ferritin, CRP and VEGF with HOMA in HIV/AIDS patients treated with combined antiretroviral therapy (cART).

MATERIALS AND METHODS:

Patients characteristics:

This cross-sectional study included 64 HIV/AIDS patients, all Caucasians, receiving cART at the HIV/AIDS Centre, Belgrade, Serbia. PAI-1, leptin, ferritin and insulin levels were measured using the Metabolic Syndrome Array I (Randox Laboratories Ltd., London, UK), while adiponectin and resistin levels were measured using Metabolic Syndrome Array II (Randox Laboratories Ltd., London, UK), interleukins (IL-1 α , IL-1 β , IFN γ , IL-2, IL-4, IL-6, IL-8, IL-10), MCP-1, TNF- α as well as VEGF was measured using Cytokine Array I (Randox Laboratories Ltd., London, UK). Insulin resistance was determined using the homeostasis model assessment index (HOMA). All biochemical analyses were performed at the Department of Clinical Biochemistry, Royal Free Hospital London, United Kingdom. The study was approved by the Ethical Committee of the School of Medicine, University of Belgrade.

Statistical analysis:

Data are presented as count (%) or median depending on data type. Association between numerical variables were explored using Spearman correlation. A linear regression model was performed in order to evaluate independent association of PAI and HOMA, adjusted for other univariate variables. All *p* values less than 0.05 were considered significant.

RESULTS:

Correlation analysis revealed significant correlations between HOMA and waist circumference, body mass index, patients' age, number of cART combinations and triglycerides ($p=0.001$, $p=0.001$, $p=0.050$, $p=0.044$, $p=0.002$, respectively). HOMA negatively correlated with levels of high density lipoprotein (HDL) (Rho=-0.282; $p=0.025$). PAI-1 (Rho= 0.334; $p=0.007$) and leptin (Rho=0.492; $p=0.001$) together with ferritin (Rho=0.396, $p=0.001$) levels positively and significantly correlated with HOMA. Levels of IL-1 α , IL-1 β , IFN γ , IL-2, IL-4, IL-6, IL-8, IL-10, adiponectin, MCP-1, resistin, TNF α , CRP and VEGF did not significantly correlate with HOMA. Further, multiple logistic regression showed that there is a statistically significant correlation between PAI, leptin and ferritin with HOMA levels ($p=0.042$; $p<0.001$, $p=0.009$, respectively).

TABLE 1. METABOLIC VARIABLES AND ADIPOCYTOKINES LEVELS IN HIV/AIDS PATIENTS

Variables, units	Median (75 th – 25 th percentile)
HOMA (μ U/L)	1.89 (1.11 - 2.68)
PAI-1, (ng/ml)	19.81 (15.89 – 24.02)
Leptin, (ng/ml)	1.43 (0.91 – 3.05)
Ferritin, (ng/ml)	114.72 (68.18 – 208.53)
IL-2, (pg/mL)	2.76 (2.22 - 3.63)
IL-4, (pg/mL)	2.58 (2.23 - 3)
IL-6, (pg/mL)	14.36 (11.31 - 21.6)
IL-8, (pg/mL)	0.85 (0.65 - 1.13)
IL-10, (pg/mL)	86.77 (58.14 - 172.19)
VEGF, (pg/mL)	86.77 (58.14 - 172.19)
TNF α , (pg/mL)	3.45 (2.73 - 4.39)
IL-1 α , (pg/mL)	0.17 (0.14 - 0.21)
IL-1 β , (pg/mL)	1.63 (1.32 - 2.23)

TABLE 2. CORRELATION BETWEEN HOMA AND INVESTIGATED PARAMETERS IN HIV/AIDS PATIENTS

Parameters	Spearman correlation	P value
WC,(cm)	0.524	0.001
BMI, (kg/m ²)	0.497	0.001
Age, (years)	0.246	0.050
AST, (IU/L)	0.139	0.272
ALT, (IU/L)	0.088	0.215
ALP, (IU/L)	0.036	0.780
TG, (mmol/L)	0.375	0.002
Total chol. (mmol/L)	-0.066	0.604
HDL, (mmol/L)	-0.282	0.025
LDL, (mmol/L)	-0.160	0.210
IL-2, (pg/mL)	0.061	0.633
IL-4, (pg/mL)	-0.071	0.581
IL-6, (pg/mL)	0.104	0.419
IL-8, (pg/mL)	0.055	0.670
IL-10, (pg/mL)	-0.121	0.346
VEGF, (pg/mL)	0.241	0.057
IFN γ , (pg/mL)	0.045	0.728
TNF α , (pg/mL)	-0.026	0.840
IL-1 α , (pg/mL)	-0.140	0.275
IL-1 β , (pg/mL)	-0.047	0.714
MCP1, (pg/mL)	-0.100	0.434
ADPN, (ng/mL)	-0.207	0.107
Retn, (ng/mL)	0.132	0.299
CRP, (mg/L)	0.015	0.906
PAI-1, (ng/mL)	0.334	0.007
LEP, (ng/mL)	0.492	0.001
Ferritin, (ng/mL)	0.396	0.001

TABLE 3. MULTIPLE REGRESSION ANALYSIS OF THE ASSOCIATION OF PAI-1 WITH HOMA

	Beta (95% CI)	Std β	P value
PAI-1	0.14 (0.001 - 0.027)	0.203	0.042
Log Leptin	0.592 (0.384 - 0.801)	0.538	< 0.001
Ferritin	0.001 (0.001 - 0.002)	0.262	0.009

CONCLUSION:

In accordance with our knowledge we showed for the first time significant correlation between PAI-1, leptin and ferritin, independently of each other with HOMA, in HIV/AIDS patients on cART.